Amendments to the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original): A Neisserial bleb preparation derived from a neisserial strain with an L2 LOS immunotype or a neisserial strain with an L3 LOS immunotype and wherein the strain is lgtB$^-$; or a Neisserial bleb preparation comprising a combination of blebs derived from a neisserial strain with an L2 LOS immunotype and a neisserial strain with an L3 LOS immunotype, optionally wherein each strain is lgtB$^-$.

2. (Currently amended): The Neisserial bleb preparation of claim 1, ~~wherein~~ comprising a ~~the~~ neisserial strain~~(s) are~~ selected from the group of a meningococcal~~,~~ ~~preferably~~ strain and a strain of serogroup B.

3. (Currently amended): The Neisserial bleb preparation of claim 1 ~~or 2~~, wherein the neisserial strain(s) cannot ~~synthesise~~ synthesize capsular polysaccharide.

4. (Currently amended): The Neisserial bleb preparation of claim 3, wherein the neisserial strain(s) have at least one of the following capsular polysaccharide genes downregulated in expression, ~~and preferably deleted~~, or deleted compared to the native strain(s) from which they are derived selected from the group of: ctrA, ctrB, ctrC, ctrD, synA, synB, synC, ~~or, preferably,~~ and saiD; and wherein L2 and L3 blebs are both present, and optionally the strains from which they are derived ~~preferably~~ have the same capsular polysaccharide gene downregulated in expression in each strain.

5. (Currently amended): The Neisserial bleb preparation of ~~claims 1-4~~ claim 1, wherein the neisserial strain(s) have either or both of the following lipid A genes downregulated in expression, ~~and preferably~~ or deleted, compared to the native strain(s) from which they are derived: msbB or htrB~~, preferably the former~~; and wherein ~~where~~ L2 and L3 blebs are both present; and optionally the strains from which they are derived ~~preferably~~ have the same lipid A gene(s) downregulated in expression in each strain.

6. (Currently amended): The Neisserial bleb preparation of ~~claims 1-5~~ claim 1, wherein the neisserial strain(s) have 1 or more of the following outer membrane protein genes downregulated in expression~~, and preferably~~ or deleted, compared to the native strain(s) from which they are derived: porA, porB, opA, opC, pilC or frpB; and wherein where L2 and L3 blebs are both present, and optionally the strains from which they are derived preferably have the same outer membrane protein gene(s) downregulated in expression in each strain.

7. (Currently amended): The Neisserial bleb preparation of claim 6, wherein the neisserial strain(s) have any of the following combinations of outer membrane protein genes downregulated in expression, ~~and preferably~~ or deleted, compared to the native strain(s) from which they are derived: PorA and OpA, PorA and OpC, OpA and OpC, PorA and OpA and OpC, PorA and FrpB, OpC and FrpB, OpA and FrpB, PorA and OpA and OpC and FrpB.

8. (Currently amended): The Neisserial bleb preparation of ~~claims 1-7~~ claim 1, wherein the neisserial strain(s) have 1 or more of the following outer membrane protein antigens upregulated in expression: NspA, TbpA low, TbpA high, Hsf, Hap, OMP85, PilQ, NadA, LbpA, MltA; and wherein where L2 and L3 blebs are both present, and optionally the strains from which they are derived ~~preferably~~ have one or more different outer membrane protein antigens upregulated in expression in each strain.

9. (Currently amended): A Neisserial bleb preparation derived from a neisserial strain which has had 2 or more of the following outer membrane proteins downregulated in expression, ~~and preferably~~ or deleted, compared to the native strain from which it is derived: PorA, PorB, OpA, OpC, PilC, or FrpB.

10. (Currently amended): The Neisserial bleb preparation of claim 9, wherein the neisserial strain has had any of the following combinations of outer membrane proteins downregulated in expression, ~~and preferably~~ or deleted, compared to the native strain from which it is derived: PorA and OpA, PorA and OpC, OpA and OpC, PorA

and OpA and OpC, PorA and FrpB, OpC and FrpB, OpA and FrpB, PorA and OpA and OpC and FrpB.

11. (Currently amended): The Neisserial strain(s) from which the Neisserial bleb preparations of ~~claims 1-10 are~~ claim 1 is derived.

12. (Currently amended): A LOS preparation isolated from the Neisserial strain(s) of claim 11 comprising immunotype L2 ~~and/~~or L3 LOS.

13. (Original): The LOS preparation of claim 12 in a liposome formulation.

14. (Currently amended): The Neisserial bleb preparation of ~~any one of claims 1-10~~ claim 1 or the LOS preparation of claim 12 ~~or 13~~, wherein the LOS contained therein is conjugated to a source of T-helper epitopes~~, preferably a protein or outer membrane protein~~.

15. (Currently amended): The Neisserial bleb preparation of claim 14 ~~which is obtainable~~ obtained through a process of intra-bleb cross-linking.

16. (Currently amended): An immunogenic composition or vaccine comprising the Neisserial bleb preparation or the LOS preparation of ~~any one of claims 1-10~~ claim 1 ~~or 12-15~~, and a pharmaceutically acceptable excipient.

17. (Currently amended): The vaccine of claim 16, ~~additionally~~ comprising an adjuvant, preferably aluminium hydroxide, or 3D-MPL and aluminium phosphate.

18. (Currently amended): The vaccine of claim 16 ~~or 17 additionally~~ comprising one or more conjugated capsular polysaccharides or oligosaccharides derived from the ~~following~~ strains selected from the group of: meningococcus serogroup A, meningococcus serogroup C, meningococcus serogroup W-135, meningococcus serogroup Y, and *H. influenzae* type b.

19. (Currently amended): A process of manufacturing the Neisserial bleb preparation vaccine of claim 16 comprising the steps of culturing the Neisserial strain(s) of claim 11, isolating blebs therefrom, optionally combining L2 and L3 blebs ~~if appropriate~~, and formulating the blebs with a pharmaceutically acceptable excipient.

20. (Currently amended): The process of claim 19, wherein the isolation step is carried out by extracting with 0.1%, about 0-0.5, about 0.02-0.4, about 0.04-0.3, about 0.06-0.2, or about 0.08-0.15% deoxycholate~~, preferably with around or exactly 0.1% deoxycholate~~.

21. (Currently amended): A bleb preparation from a Gram-negative bacterial strain comprising an outer-membrane protein conjugated to LOS integrated in the outer-membrane ~~of which is integrated an outer-membrane protein conjugated to LOS~~.

22. (Currently amended): The bleb preparation of claim 21, wherein more than 10, 20, 30, 40, 50, 60, 70, 80, 90, 95 or 99% of the conjugated LOS has ~~its~~ a lipid A moiety integrated in the outer-membrane of the bleb ~~and/~~or in an environment whereby its toxicity is reduced or shielded from a host to which it has been administered.

23. (Currently amended): The bleb preparation of claim 21 ~~or 22~~, wherein the toxicity of the LOS in the bleb is reduced compared to the blebs with the same amount of unconjugated LOS.

24. (Currently amended): The bleb preparation of ~~claims 21-23~~ claim 21, wherein more than 10, 20, 30, 40, 50, 60, 70, 80, 90, 95 or 99% of the conjugated LOS is in a native conformation that induces ~~suitable for inducing~~ a bactericidal antibody response against it when administered to a host's immune system.

25. (Currently amended): The bleb preparation of ~~claims 21-24~~ claim 21, wherein the conjugated LOS has a conformation that elicits ~~suitable for eliciting~~ an immune response in a host reactive against unconjugated LOS.

26. (Currently amended): The bleb preparation of ~~claims 21-25~~ claim 21, wherein the outer-membrane protein is conjugated to the oligosaccharide or polysaccharide moiety of the LOS molecule.

27. (Currently amended): The bleb preparation of claim 21~~-26~~, wherein the outer-membrane protein and LOS molecule are native to the Gram-negative bacterial strain from which the blebs are derived.

28. (Currently amended): The bleb preparation of ~~claims 21-27~~ claim 21 obtained ~~obtainable~~ by a process of intra-bleb cross-linking.

29. (Currently amended): The bleb preparation of ~~claims 21-28~~ claim 21 wherein more than 10, 20, 30, 40, 50, 60, 70, 80, 90, or 95% of the LOS present in the blebs is cross-linked or conjugated to outer membrane protein.

30. (Currently amended): The bleb preparation of ~~claims 21-29~~ claim 21 derived from a Gram-negative strain that does not produce capsular polysaccharide, or from a bleb preparation that does not comprise capsular polysaccharide.

31. (Currently amended): The bleb preparation of ~~claims 21-30~~ claim 21, wherein capsular polysaccharide is not conjugated to an outer-membrane protein integrated in the bleb preparation.

32. (Currently amended): The bleb preparation of ~~claims 21-31~~ claim 21 derived from a *Moraxella catarrhalis* or a non-typeable *Haemophilus influenzae* strain.

33. (Currently amended): The bleb preparation of ~~claims 21-31~~ claim 21 derived from a strain selected from the group of a Neisserial strain and ~~, preferably~~ *Neisseria meningitis.*

34. (Currently amended): The bleb preparation of claim 33, wherein the bleb preparation comprises conjugated L2 LOS, conjugated L3 LOS, or a mixture of

conjugated L2 and L3 LOS optionally ~~preferably~~ separately conjugated to at least 2 different blebs.

35. (Currently amended): The bleb preparation of claim 33 ~~or 34~~ derived from lgtB$^-$ strains, or wherein the LOS has a truncated structure consistent with it having been derived from a strain which is lgtB$^-$.

36. (Currently amended): The bleb preparation of ~~claims 32-35~~ claim 32, derived from htrB$^-$ ~~and/~~or msbB$^-$ strains, or wherein the LOS Lipid A moiety lacks secondary acyl chains consistent with it having been isolated from a htrB$^-$ ~~and/~~or msbB$^-$ meningococcal strain.

37. (Currently amended): An immunogenic composition or vaccine comprising the bleb preparation of ~~claims 21-36~~ claim 21, and a pharmaceutically acceptable excipient.

38. (Currently amended): The immunogenic composition or vaccine of claim 37 additionally comprising an adjuvant~~, preferably aluminium hydroxide, or 3D-MPL and aluminium phosphate~~.

39. (Currently amended): The immunogenic composition or vaccine of claim 37 ~~or 38 additionally~~ comprising one or more conjugated capsular polysaccharides or oligosaccharides derived from the following strains: meningococcus serogroup A, meningococcus serogroup C, meningococcus serogroup W-135, meningococcus serogroup Y, and *H. influenzae* type b.

40. (Currently amended): A process of producing an intra-bleb conjugated bleb preparation from a Gram-negative bacterial strain comprising an outer-membrane protein conjugated to LOS integrated in the outer-membrane ~~of which is integrated an outer-membrane protein conjugated to LOS~~, comprising the steps of:

a) isolating blebs from the Gram-negative strain,

b) carrying out a method ~~chemistry suitable~~ for conjugating the oligosaccharide moiety of the LOS present in the blebs to an outer membrane protein present on the same bleb,

c) isolating the intra-bleb conjugated bleb preparation, and

d) optionally formulating the intra-bleb conjugated bleb preparation with a further intra-bleb conjugated bleb preparation made by the same process but having a different LOS immunotype and optionally ~~and/or~~ formulating the bleb preparation with a pharmaceutically acceptable excipient to make a vaccine composition.

41. (Currently amended): The process of claim 40 wherein step a) the blebs are extracted using a ~~low concentration~~ of deoxycholate of about ~~such as~~ 0-0.3%, or about or exactly ~~preferably around or exactly~~ 0.1%.

42. (Currently amended): The process of claim 40 ~~or 41~~, wherein in step b) the pH is kept between 7 and 9, or at ~~preferably~~ around pH 7.5.

43. (Currently amended): The process of ~~claims 40-42~~ claim 40, wherein step b) is carried out in about 1-5% sucrose~~, preferably around 3%~~.

44. (Currently amended): The process of ~~claims 40-43~~ claim 40, wherein step b) is carried out in low NaCl concentration conditions.

45. (Currently amended): The process of ~~claims 40-44~~ claim 40, wherein step b) is carried out with a method comprising EDAC/NHS chemistry.

46. (Currently amended): The process of ~~claims 40-45~~ claim 40, wherein in step a) the blebs are isolated from a strain selected from the group of a neisserial strain, ~~preferably~~ a meningococcal strain, and a ~~most preferably a~~ meningococcus B strain.

47. (Currently amended): The process of claim 46 wherein the strain is selected from the group of one that cannot make capsular polysaccharide, and ~~is preferably a saiD~~ a mutant strain.

48. (Currently amended): The process of claim 46 ~~or 47~~ wherein the strain is an lgtB$^-$ mutant.

49. (Currently amended): The process of ~~claims 46-48~~ claim 46 wherein the strain is msbB$^-$ ~~and/~~or htrB$^-$.

50. (Currently amended): The process of ~~claims 46-49~~ claim 46 wherein the strain has an L2 LOS immunotype.

51. (Currently amended): The process of ~~claims 46-50~~ claim 46 wherein the strain has an L3 LOS immunotype.

52. (Currently amended): The process of ~~claims 46-51~~ claim 46 wherein in step d) a meningococcal intra-bleb conjugated bleb preparation with an L2 immunotype made by the process of claim 50 is combined with a further meningococcal intra-bleb conjugated bleb preparation with an L3 immunotype ~~made by the process of claim 51~~.

53. (New): The Neisserial bleb preparation of claim 14 wherein the source of T-helper epitopes comprises a protein or outer membrane protein.

54. (New): The process of claim 46 wherein in step d) a meningococcal intra-bleb conjugated bleb preparation with an L2 immunotype is combined with a further meningococcal intra-bleb conjugated bleb preparation with an L3 immunotype made by the process of claim 51.

55. (New) The immunogenic composition or vaccine of claim 38 wherein the adjuvant is aluminum hydroxide or 3D-MPL and aluminum phosphate.